

ATTORNEY'S DOCKET NO: M0656/7070(HCL)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Liu et al.  
Serial No: 09/982,548  
Filed: October 18, 2001  
For: METHODS AND PRODUCTS RELATED TO PULMONARY  
DELIVERY OF POLYSACCHARIDES  
Examiner: Unassigned  
Art Unit: 1623

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Helen C. Lockhart

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Commissioner for Patents  
Washington, D.C. 20231

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STATEMENT FILED PURSUANT TO THE DUTY OF  
DISCLOSURE UNDER 37 CFR §§1.56, 1.97 AND 1.98

Sir:

Pursuant to the duty of disclosure under 37 C.F.R. §§1.56, 1.97 and 1.98, the Applicant requests consideration of this Information Disclosure Statement.

PART I: Compliance with 37 C.F.R. §1.97

This Information Disclosure Statement has been filed within three months of the filing date of a National Application.

No fee or certification is required.

PART II: Information Cited

The Applicant hereby makes of record in the above-identified application the information listed on the attached form PTO-1449 (modified). The order of presentation of the references should not be construed as an indication of the importance of the references.

The applicant would like to bring to the Examiner's attention the following co-pending applications that may contain subject matter related to this application:

<u>Docket No.</u>	<u>Serial No.</u>	<u>Filing Date</u>	<u>Inventor(s)</u>
M0656/7046	09/384,959	08/27/99	Sasisekharan et al.
M0656/7055	09/557,997	04/24/00	Venkataraman et al.
M0656/7056	09/558,137	04/24/00	Venkataraman et al.
M0656/7063	09/802,285	03/08/01	Liu et al.
M0656/7069	09/951,138	09/12/01	Sasisekharan et al.

The following are remarks concerning the other information cited:

PART III: Remarks

Documents cited on the attached form PTO-1449 (modified) are enclosed unless otherwise indicated on the attached form PTO-1449 (modified). It is respectfully requested that:

1. The Examiner consider completely the cited information, along with any other information, in reaching a determination concerning the patentability of the present claims;
2. The enclosed form PTO-1449 be signed by the Examiner to evidence that the cited information has been fully considered by the Patent and Trademark Office during the examination of this application;
3. The citations for the information be printed on any patent which issues from this application.

By submitting this Information Disclosure Statement, the Applicant makes no representation that a search has been performed, of the extent of any search performed, or that more relevant information does not exist.

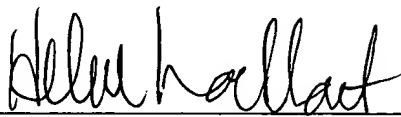
By submitting this Information Disclosure Statement, the Applicant makes no representation that the information cited in the Statement is, or is considered to be, material to patentability as defined in 37 C.F.R. §1.56(b).

By submitting this Information Disclosure Statement, the Applicant makes no representation that the information cited in the Statement is, or is considered to be, in fact, prior art as defined by 35 U.S.C. §102.

Notwithstanding any statements by the Applicant, the Examiner is urged to form his own conclusion regarding the relevance of the cited information.

An early and favorable action is hereby requested.

Respectfully submitted,  
*Liu et al., Applicant(s)*

By:   
Helen C. Lockhart, Reg No. 39,248  
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600 Atlantic Avenue  
Boston, MA 02210  
Telephone (617) 720-3500

Docket No. M0656/7070(HCL)  
Dated: January 17, 2002  
**X01/18/01**



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ATTORNEY'S DOCKET NO. M0656/7070(HCL)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s): Liu et al.  
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Helen C. Lockhart

COMMISSIONER FOR PATENTS  
WASHINGTON, D.C. 20231

Sir:

Transmitted herewith is/are the following document(s):

- ☒ Information Disclosure Statement
- ☒ Form PTO1449 with Cited References
- ☒ Certificate of Mailing
- ☒ Return Receipt Postcard

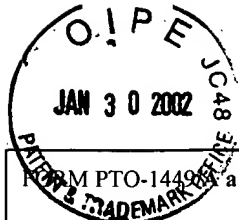
If the enclosed papers are considered incomplete, the Mail Room and/or the Application Branch is respectfully requested to contact the undersigned at (617) 720-3500, Boston, Massachusetts.

No check is enclosed. If a fee is required, the balance may be charged to the account of the undersigned, Deposit Account No. 23/2825. A duplicate of this sheet is enclosed.

Respectfully Submitted,

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Docket No. M0656/7070(HCL)  
Date: January 17, 2002  
X01/18/02



FORM PTO-1449a and B (Modified) <b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>		APPLICATION NO.: 09/982,548	ATTY. DOCKET NO.: M0656/7070
		FILING DATE: October 18, 2001	
		APPLICANT: Liu et al.	
		GROUP ART UNIT: 1623	EXAMINER: Unassigned
Sheet	1	of	4

**U.S. PATENT DOCUMENTS**

Examiner's Initials#	Cite No.	U.S. Patent Document		Name of Patentee or Applicant of Cited Document	Date of Publication or of issue of Cited Document MM-DD-YYYY
		Number	Kind Code		
	A1	4,281,108	B1	Fussi	07/28/1981
	A2	4,341,869	B1	Langer, Jr. et al.	07/27/1982
	A3	4,373,023	B1	Langer et al.	02/08/1983
	A4	4,396,762	B1	Langer et al.	08/02/1983
	A5	4,443,545	B1	Langer, Jr. et al.	04/17/1984
	A6	4,745,105	B1	Griffin et al.	05/17/1988
	A7	4,757,056	B1	Van Gorp et al.	07/12/1988
	A8	4,942,156	B1	Foley et al.	07/17/1990
	A9	4,990,502	B1	Lormeau et al.	02/05/1991
	A10	5,010,063	B1	Piani et al.	04/23/1991
	A11	5,039,529	B1	Bergendal et al.	08/13/1991
	A12	5,106,734	B1	Nielsen	04/21/1992
	A13	5,152,784	B1	Tsilibary	10/06/1992
	A14	5,164,378	B1	Conti et al.	11/17/1992
	A15	5,169,772	B1	Zimmerman et al.	12/08/1992
	A16	5,204,323	B1	Findlay et al.	04/20/1993
	A17	5,252,339	B1	Cristofori et al.	10/12/1993
	A18	5,262,325	B1	Zimmermann et al.	11/16/1993
	A19	5,290,695	B1	Morikawa et al.	03/01/1994
	A20	5,338,677	B1	Zimmermann et al.	08/16/1994
	A21	5,389,539	B1	Sasisekharan et al.	02/14/1995
	A22	5,474,987	B1	Cohen et al.	12/12/1995
	A23	5,567,417	B1	Sasisekharan et al.	10/22/1996
	A24	5,569,600	B1	Sasisekharan et al.	10/29/1996
	A25	5,576,304	B1	Kakkar et al.	11/19/1996
	A26	5,599,801	B1	Branellec et al.	02/04/1997
	A27	5,618,917	B1	Toback et al.	04/08/1997
	A28	5,619,421	B1	Venkataraman et al.	04/08/1997
	A29	5,681,733	B1	Su et al.	10/28/1997
	A30	5,714,376	B1	Sasisekharan et al.	02/03/1998
	A31	5,744,515	B1	Clapper	04/28/1998
	A32	5,753,445	B1	Fillit et al.	05/19/1998
	A33	5,763,427	B1	Weitz et al.	06/09/1998
	A34	5,776,434	B1	Purewal et al.	07/07/1998
	A35	5,795,875	B1	Holme et al.	08/18/1998
	A36	5,808,021	B1	Holme et al.	09/15/1998
	A37	5,824,299	B1	Luster et al.	10/20/1998

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	A38	5,830,726	B1	Sasisekharan et al.	11/03/1998
	A39	5,855,913	B1	Hanes et al.	01/05/1999
	A40	5,874,064	B1	Edwards et al.	02/23/1999
	A41	5,879,713	B1	Roth et al.	03/09/1999
	A42	5,919,693	B1	Su et al.	07/06/1999
	A43	5,922,358	B1	Doutremepuich et al.	07/13/1999
	A44	5,968,822	B1	Pecker et al.	10/19/1999
	A45	5,985,309	B1	Edwards et al.	11/16/1999
	A46	5,997,863	B1	Zimmermann et al.	12/07/1999
	A47	6,013,628	B1	Skubitz et al.	01/11/2000
	A48	6,116,237	B1	Schultz et al.	09/12/2000
	A49	6,136,295	B1	Edwards et al.	10/24/2000
	A50	RE37,053	B1	Hanes et al.	02/13/2001
	A51	6,217,863	B1	Godavarti et al.	04/17/2001

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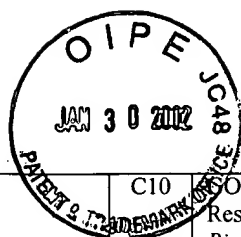
#### FOREIGN PATENT DOCUMENTS

Examiner's Initials#	Cite No.	Foreign Patent Document			Name of Patentee or Applicant of Cited Document (not necessary)	Date of Publication of Cited Document MM-DD-YYYY	Translation (Y/N)
		Office/ Country	Number	Kind Code			
	B1	EP	0 433 225	A1	CIBA-GEIGY AG	06/19/1991	
	B2	WO	93/08289	A1	Massachusetts Institute of Technology	04/29/1993	
	B3	EP	0 557 887	A2	OPOCRIN S.p.A.	09/01/1993	
	B4	WO	93/19096	A1	Cancer Research Campaign Technology	09/30/1993	
	B5	WO	94/21689	A1	Cancer Research Campaign Technology	09/29/1994	
	B6	WO	95/34635	A1	IBEX Technologies	12/21/1995	
	B7	WO	97/16556	A1	Massachusetts Institute of Technology	05/09/1997	
	B8	WO	00/12726	A2	Massachusetts Institute of Technology	03/09/2000	
	B9	WO	00/65521	A2	Massachusetts Institute of Technology	11/02/2000	

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#### OTHER ART — NON PATENT LITERATURE DOCUMENTS

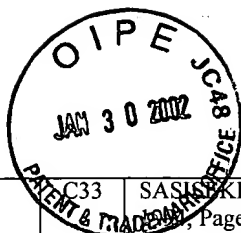
Examiner's Initials#	Cite No	Include name of the author (in CAPITAL LETTERS) title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, relevant page(s), volume-issue number(s), publisher, city and/or country where published.	Translation (Y/N)
	C1	ALDERMAN, C.P. et al., "Continuous Subcutaneous Heparin Infusion for Treatment of Trousseau's Syndrome", <i>The Annals of Pharmacotherapy</i> , July/August 1995, Pages 710-713, Vol. 29	
	C2	BERNSTEIN, H. et al., "Immobilized Heparin Lyase System for Blood Deheparinization", <i>Methods in Enzymology</i> , 1988, Pages 515-529, Vol. 137, Academic Press, Inc.	
	C3	CARDIN, A.D. et al., "Molecular Modeling of Protein-Glycosaminoglycan Interactions", <i>Arteriosclerosis</i> , January/February 1989, Pages 21-32, Vol. 9, No. 1	
	C4	COMFORT, A.R. et al., "Immobilized Enzyme Cellulose Hollow Fibers: III. Physical Properties and <i>In Vitro</i> Biocompatibility", <i>Biotechnology and Bioengineering</i> , 1989, Pages 1383-1390, Vol. 34, John Wiley & Sons, Inc.	
	C5	EDWARDS, D.A. et al., "Large Porous Particles for Pulmonary Drug Delivery", <i>Science Reprint Series</i> , June 20, 1997, Pages 1868-1871, Vol. 276, American Association for the Advancement of Science	
	C6	EDWARDS, D.A. et al., "Recent advances in pulmonary drug delivery using large, porous inhaled particles", <i>J. Appl. Physiol.</i> , August 1998, Pages 379-385, Vol. 85, No. 2, American Physiological Society	
	C7	ENRIQUEZ-HARRIS, P. et al., "Growth factors and the extracellular matrix", <i>Meeting Report, Trends in Cell Biology</i> , 1994, 2 Pages	
	C8	ERNST, S. et al., "Direct evidence for a predominantly exolytic processive mechanism for depolymerization of heparin-like glycosaminoglycans by heparinase I", <i>Proc. Natl. Acad. Sci. USA</i> , April 1998, Pages 4182-4187, Vol. 95	
	C9	FEINGOLD, D.S. et al., "Conformational aspects of the reaction mechanisms of polysaccharide lyases and epimerases", <i>FEB Letters</i> , November 1987, Pages 207-211, Vol. 223, No. 2, Elsevier Science Publishers B.V.	



C10	GODAVARTI, R. et al., "Heparinase I from <i>Flavobacterium heparinum</i> . Identification of a Critical Histidine Residue Essential for Catalysis as Probed by Chemical Modification and Site-Directed Mutagenesis", <i>Biochemistry</i> , 1996, Pages 6846-6852, Vol. 35, No. 21, American Chemical Society	TECH CENTER 1600/2900	FEB 01 2002
C11	GODAVARTI, R. et al., "Heparinase III for <i>Flavobacterium heparinum</i> : cloning and recombinant expression in <i>Escherichia coli</i> ", <i>Biochem. Biophys. Res. Commun.</i> , August 23, 1996, Pages 751-758, Vol. 225, No. 3, Academic Press, Inc.		
C12	GODAVARTI, R. et al., "A comparative analysis of the primary sequences and characteristics of heparinases I, II, and III from <i>Flavobacterium heparinum</i> ", <i>Biochem. Biophys. Res. Commun.</i> , December 24, 1996, Pages 770-777, Vol. 229, No. 3, Academic Press, Inc.		
C13	HARENBERG, J. et al., "Anticoagulant effects and tissue factor pathway inhibitor after intrapulmonary low-molecular-weight heparin", <i>Blood Coagulation and Fibrinolysis</i> , 1996, Pages 477-482, Vol. 7, Rapid Science Publishers		
C14	HART, G.W., "Glycosylation", <i>Current Opinion in Cell Biology</i> , 1992, Pages 1017-1023, Vol. 4		
C15	HUANG, J.N. et al., "Low-Molecular-Weight Heparins", <i>Hematology/Oncology Clinics of North America</i> , December 1998, Pages 1251-1281, Vol. 12, No. 6		
C16	JACKSON, R.L. et al., "Glycosaminoglycans: Molecular Properties, Protein Interactions, and Role in Physiological Processes", <i>Physiological Reviews</i> , April 1991, Pages 481-539, Vol. 71, No. 2, The American Physiological Society	DECEMBER 1998	2002
C17	KAKKAR, A.K. et al., "Venous thromboembolism and cancer", <i>Baillier's Clinical Haematology</i> , September 1998, Pages 675-687, Vol. 11, No. 3, Bailliere Tindall		
C18	KANABROCKI, E.L. et al., "Heparin as a Therapy for Atherosclerosis: Preliminary Observations on the Intrapulmonary Administration of Low-Dose Heparin in the Morning Versus Evening Gauged by Its Effect on Blood Variables", <i>Chronobiology International</i> , 1991, Pages 210-233, Vol. 8, No. 3, International Society of Chronobiology		
C19	KANABROCKI, E.L. et al., "A Quest for the Relief of Atherosclerosis: Potential Role of Intrapulmonary Heparin - A Hypothesis", <i>Quarterly Journal of Medicine</i> , April 1992, Pages 259-282, New Series 83, No. 300, Oxford University Press		
C20	KRETSINGER, R.H. et al., "Structure and Evolution of Calcium-Modulated Proteins", <i>CRC Critical Reviews in Biochemistry</i> , July 1980, Pages 119-174, Vol. 8, No. 2		
C21	LECKBAND, D. et al., "An Approach for the Stable Immobilization of Proteins", <i>Biotechnology and Bioengineering</i> , 1991, Pages 227-237, Vol. 37, John Wiley & Sons, Inc.		
C22	LINHARDT, R.J. et al., "Polysaccharide Lyases", <i>Applied Biochemistry and Biotechnology</i> , 1986, Pages 135-176, Vol. 12		
C23	LINHARDT, R.J. et al., "Examination of the Substrate Specificity of Heparin and Heparan Sulfate Lyases", <i>Biochemistry</i> , 1990, Pages 2611-2617, Vol. 29, No. 10, American Chemical Society		
C24	LINHARDT, R.J. et al., "Production and Chemical Processing of Low Molecular Weight Heparins", <i>Seminars in Thrombosis and Hemostasis</i> , 1999, Pages 5-16, Vol. 25, Suppl. No. 3, Thiemo Medical Publishers, Inc.		
C25	LIU, D. et al., "The Calcium-binding Sites of Heparinase I from <i>Flavobacterium heparinum</i> are Essential for Enzymatic Activity", <i>The Journal of Biological Chemistry</i> , February 12, 1999, Pages 4089-4095, Vol. 274, No. 7, The American Society for Biochemistry and Molecular Biology, Inc.		
C26	LIU, J. et al., "Heparan Sulfate D-Glucosaminyl 3-O-Sulfotransferase-3A Sulfates N-Unsubstituted Glucosamine Residues", <i>The Journal of Biological Chemistry</i> , December 31, 1999, Pages 38155-38162, Vol. 274, No. 53, The American Society for Biochemistry and Molecular Biology, Inc.		
C27	LOHSE, D.L. et al., "Purification and Characterization of Heparin Lyases from <i>Flavobacterium heparinum</i> ", <i>The Journal of Biological Chemistry</i> , December 5, 1992, Pages 24347-24355, Vol. 267, No. 34, The American Society for Biochemistry and Molecular Biology, Inc.		
C28	LUSTIG, F. et al., "Alternative Splicing Determines the Binding of Platelet-Derived Growth Factor (PDGF-AA) to Glycosaminoglycans", <i>Biochemistry</i> , 1996, Pages 12077-12085, Vol. 35, No. 37, American Chemical Society		
C29	POJASEK, K. et al., "Histidine 295 and histidine 510 are crucial for the enzymatic degradation of heparan sulfate by heparinase III", <i>Biochemistry</i> , April 11, 2000, Pages 4012-4019, Vol. 39, No. 14, American Chemistry Society		
C30	RHOMBERG, A.J. et al., "Mass spectrometric and capillary electrophoretic investigation of the enzymatic degradation of heparin-like glycosaminoglycans", <i>Proc. Natl. Acad. Sci. USA</i> , April 1998, Pages 4176-4181, Vol. 95		
C31	RHOMBERG, A.J. et al., "Mass spectrometric evidence for the enzymatic mechanism of the depolymerization of heparin-like glycosaminoglycans by heparinase II", <i>Proc. Natl. Acad. Sci. USA</i> , October 1998, Pages 12232-12237, Vol. 95		
C32	SASISEKHARAN, R. et al., "Cloning and expression of heparinase I gene from <i>Flavobacterium heparinum</i> ", <i>Proc. Natl. Acad. Sci. USA</i> , April 1993, Pages 3660-3664, Vol. 90, Applied Biological Sciences		

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C33	SASISEKHARAN, R. et al., "Heparinase inhibits neovascularization", <i>Proc. Natl. Acad. Sci. USA</i> , February 1995, Pages 1524-1528, Vol. 91		
C34	SASISEKHARAN, R. et al., "Heparinase I from <i>Flavobacterium heparinum</i> : The Role of the Cysteine Residue in Catalysis as Probed by Chemical Modification and Site-Directed Mutagenesis", <i>Biochemistry</i> , 1995, Pages 14441-14448, Vol. 34, No. 44, American Chemical Society		
C35	SASISEKHARAN, R. et al., "Heparinase I from <i>Flavobacterium heparinum</i> , Mapping and Characterization of the Heparin Binding Domain", <i>The Journal of Biological Chemistry</i> , February 9, 1996, Pages 3124-3131, Vol. 271, No. 6, The American Society for Biochemistry and Molecular Biology, Inc.		
C36	SASISEKHARAN, R. et al., "Heparin and heparan sulfate: biosynthesis, structure and function", <i>Curr. Opin. Chem. Biol.</i> , December 2000, Pages 626-631, Vol. 4, No. 6, The American Society for Biochemistry and Molecular Biology, Inc.		
C37	SHRIVER, Z. et al., "Heparinase II from <i>Flavobacterium heparinum</i> , Role of Histidine Residues in Enzymatic Activity as Probed by Chemical Modification and Site-Directed Mutagenesis", <i>The Journal of Biological Chemistry</i> , April 24, 1998, Pages 10160-10167, Vol. 273, No. 17, The American Society for Biochemistry and Molecular Biology, Inc.		
C38	SHRIVER, Z. et al., "Heparinase II from <i>Flavobacterium heparinum</i> , Role of cysteine in Enzymatic Activity as Probed by Chemical Modification and Site-Directed Mutagenesis", <i>The Journal of Biological Chemistry</i> , September 4, 1998, Pages 22904-22912, Vol. 273, No. 36, The American Society for Biochemistry and Molecular Biology, Inc.		
C39	SHRIVER, Z. et al., "Biochemical Investigations and Mapping of the Calcium-binding Sites of Heparinase I from <i>Flavobacterium heparinum</i> ", <i>The Journal of Biological Chemistry</i> , February 12, 1999, Pages 4082-4088, Vol. 274, No. 7, The American Society for Biochemistry and Molecular Biology, Inc.		
C40	SHRIVER, Z. et al., "Sequencing of 3-O sulfate containing heparin decasaccharides with a partial antithrombin III binding site", <i>Proc. Natl. Acad. Sci. USA</i> , September 12, 2000, Pages 10359-10364, Vol. 97, No. 19		
C41	SHRIVER, Z. et al., "Cleavage of the antithrombin III binding site in heparin by heparinases and its implication in the generation of low molecular weight heparin", <i>Proc. Natl. Acad. Sci. USA</i> , September 12, 2000, Pages 10365-10370, Vol. 97, No. 19		
C42	VALENTINE, K.A. et al., "Low-Molecular-Weight Heparin Therapy and Mortality", <i>Seminars in Thrombosis and Hemostasis</i> , 1997, Pages 173-178, Vol. 23, No. 2, Thieme Medical Publishers, Inc.		
C43	VENKATARAMAN, G. et al., "Sequencing complex polysaccharides", <i>Science</i> , October 15, 1999, Pages 537-542, Vol. 286(5439)		
C44	YANG, V.C. et al., "Purification and Characterization of Heparinase from <i>Flavobacterium heparinum</i> ", <i>The Journal of Biological Chemistry</i> , February 10, 1985, Pages 1849-1857, Vol. 260, No. 3, The American Society of Biological Chemists, Inc.		
C45	ZACHARSKI, L.R. et al., "Blood Coagulation Activation in Cancer: Challenges for Cancer Treatment", <i>Hamostaseologic</i> , 1995, Pages 14-20, Vol. 15, F.K. Schattauer Verlagsgesellschaft mbH		

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EXAMINER	DATE CONSIDERED
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#EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

\*a copy of this reference is not provided as it was previously cited by or submitted to the office in a prior application, Serial No. \_\_\_\_\_, filed \_\_\_\_\_, and relied upon for an earlier filing date under 35 U.S.C. 120 (continuation, continuation-in-part, and divisional applications).

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